AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph starting on page 16, line 9 as follows:

The PACAP gene targeting vector was constructed from genomic DNA clones (λMPL4 and λMPL18) (Yamamoto, K., Hashimoto, H., Hagihara, N., Nishino, A., Fujita, T., Matsuda, T. & Baba, A. (1998) Gene 211, 63-69) isolated from a 129/SvJ mouse genomic library. A 2.1-kb PvuII fragment of the PACAP gene containing part of exon 5 and the 3' flanking region was inserted 3' to the neomycin resistant (neo) gene (derived from pGEM7-PGK-neo-polyA) in pBluescript KS(+). A MC1 promoter-driven diphtheria toxin A-fragment (DT) gene (derived from pMC1DTpA) was then inserted 5' to the neo gene. Subsequently, a 5.3-kb HindIII genomic DNA fragment containing exons 1A through 4 was inserted between the DT and neo genes, to generate the PACAP targeting vector (Fig. 1A). The linearized vector was electroporated into 129/Ola mouse-derived E14tg2a ES cells. Targeted clones were identified by Southern blot analysis using external 0.42-kb and 1.1-kb probes and microinjected into C57BL/6 E3.5 blastocysts. Two highly chimeric males showed germ-line transmission and were mated with C57BL/6 wild-type females to produce F1 heterozygous mice. F1 heterozygotes were mated with C57BL/6 mice to produce the F2- and F3-generation mice, which were used in this study unless otherwise specified. The null allele of PACAP was also backcrossed 5 times with ICR mice, whose litter sizes were much larger than C57BL/6 mice. Wild-type mice and mice homozygous for the mutant PACAP gene were

obtained from the intercross of heterozygous animals, and experiments were conducted with adult (three to five months old) mice. Reverse transcription-polymerase chain reaction (RT-PCR) was performed as described in Hashimoto, H., Hagihara, N., Koga, K., Yamamoto, K., Shintani, N., Tomimoto, S., Mori, W., Koyama, Y., Matsuda, T. & Baba, A. (2000) J. Neurochem. 74, 501-507, using the following PACAP gene exon-specific primers: exon 3, 5'-AGA AGA CGA GGC TTA CGA CCA G-3' (SEQ ID NO:1) (sense); exon 4, 5'-ACG ACC GAC TGC AGG TAC TTC-3' (SEQ ID NO:2) (antisense); and exon 5, 5'-TTT CTT GAC AGC CAT TTG TTT TCG G-3' (SEQ ID NO:3) (antisense). The β-actin housekeeping gene was simultaneously reverse transcribed and amplified as previously described in Kitanaka, J., Hashimoto, H., Sugimoto, Y., Sawada, M., Negishi, M., Suzumura, A., Marunouchi, T., Ichikawa, A. & Baba, A. (1995) Biochim. Biophys. Acta 1265, 220-223. In situ hybridization analysis was performed on parasagittal brain sections as described in Hashimoto, H., Nogi, H., Mori, K., Ohishi, H., Shigemoto, R., Yamamoto, K., Matsuda, T., Mizuno, N., Nagata, S. & Baba, A. (1996) J. Comp. Neurol. 371, 567-577. Two different cDNA fragments of mouse PACAP (Yamamoto, K., Hashimoto, H., Hagihara, N., Nishino, A., Fujita, T., Matsuda, T. & Baba, A. (1998) Gene 211, 63-69), a 431-bp cDNA fragment (-116 to 315, where +1 represents the nucleotide position of the ATG initiation codon) spanning exons 2-4, and a 198-bp fragment (340 to 537) containing part of the exon 5 coding sequence deleted by homologous recombination, were used as templates to synthesize 35S-CTP-labeled cRNA probes. The expression of the

biologically active mature PACAP isoform, PACAP38, was studied in brain by a radioimmunoassay kit (Peninsula Labs, Belmont, CA, USA).